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REMARKS

Claims 1-5, 9-14 and 18 are pending in the application. No claims have been amended. Applicants respectfully request reconsideration of this application in view of the following remarks.

Claim Allowance

Claims 1-3 and 14 were allowed. *See* the Office Action, page 7.

Claim Rejection Under 35 U.S.C. § 112, ¶1

The Examiner rejected claims 4-5, 9-13 and 18 under 35 U.S.C. § 112, ¶1, as failing to comply with the written description requirement. Claim 4 is directed to a method of treating oncoses; claim 5 is directed to a method of inhibiting mitosis; claims 9-13 are directed to a method of treating benign and oncoses; and claim 18 is directed to a method of treating tumor diseases. Applicants respectfully traverse the grounds of the Examiner's rejection as follows.

Written Description v. Enablement

Although the Examiner rejected claims 4-5, 9-13 and 18 under the written description provision of the first paragraph of 35 U.S.C. 112, the Examiner reasoned that "the claims are too broad and [the] disclosure does not provide guidance or direction for the treatment of all the diseases as claimed." *Id.* at page 5; *also see id.* at page 7. Specifically, the Examiner stated that:

> See In re Buting, 163 USPQ 689.[1] The disclosure provides no indication of whether the compounds treat all cancers. To **make clearer the lack of enablement** for treatment of all cancer, extrinsic evidence is supplied by Draetta . . . Since no universal cure for cancer has been developed, it follows that there is no correlation between the assays relied by applicants and the ability to treat all types of diseases base on rapid and uncontrolled proliferation of endogenous cells. Thus, the data as presented are not sufficient to **enable** such claims.

[1] In *In re Buting*, 163 USPQ 689 (CCPA 1969), the court addressed the issue of utility rather than written description. Specifically, the court stated that "record did not establish a credible basis for the assertion that the single class of compounds in question would be useful in treating disparate types of cancers." *Id.* at 690.

* * *

> The specification provides test data for proliferation of three disorazole compounds A1, D1 and E1, since there is no guidance and/or direction provided by the Applicants for method of treatment of oncoses . . . one skilled in the art would not **be able to make and use** the invention.
>
> The specification provides test data for proliferation of three disorazole compounds A1, D1 and E1, the claims are too broad and disclosure does not provide guidance or direction for the treatment of all the diseases as claimed. See MPEP 2163.06.[2]

Id. at pages 6-7 (emphases added). Thus, the Examiner's reasoning is based on the assertion that the specification is not enabled for the claimed methods of use.

The written description requirement is separate and distinct from the enablement requirement. *See, e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991). Moreover, "[t]he purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required to 'recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'" *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1561 (Fed. Cir. 2003). On the other hand, "[t]he enablement requirement is often more indulgent than the written description requirement. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *Genetech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361 1365 (Fed. Cir. 1997).

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[2] MPEP § 2163.06 is entitled "Relationship of Written Description Requirement to New Matter." As new matter is not an issue here, the citation is misplaced.

As set forth below, Applicants address both of written description and enablement issues with respect to the rejected claims.

Claims 4-5, 9-13 and 18

(A) WRITTEN DESCRIPTION

"The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *In re Kaslow*, 707 F.2d 1366 (Fed. Cir. 1983). As discussed below, one skilled in the art would recognize that Applicants have possession of the claimed invention.

Claim 5 is directed to a method of inhibiting mitosis in rapidly and uncontrolledly proliferating endogenous cells by administering disorazole compounds; and claims 4, 9-13 and 18 are directed methods of treating oncoses, benign or tumor diseases with disorazole compounds.

It is the Examiner's position that "the specification provides test data for proliferation of three disorazole compounds A1, D1 and E1, the claims are too broad and disclosure does not provide guidance or direction for the treatment of all the diseases as claimed." The Office Action, page 5; *also see id.* at page 7. Applicants disagree. As MPEP § 2163.II points out, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice ... A 'representative number of species' means that the species which are adequately described are representative of the entire genus." Although the specification only provides testing data for anti-proliferation of three disorazole compounds, these tested compounds share a general core structure of disorazoles, and therefore, are representative of the entire genus. Accordingly, one

skilled in the art would recognize that Applicants have possession of the claimed methods of inhibition and treatment with disorazole compounds.

Here, Applicants' possession of claim 5 is shown by describing an actual reduction to practice of using disorazole compounds to inhibit proliferative cells and inhibit the cell cycles. *See* Examples 7-10. Applicants' possession of claims 4, 9-13 and 18 is shown by describing an actual reduction to practice of using disorazole compounds, *in vitro* and *in vivo*, to inhibit proliferation, to inhibit the polymerization of tublin, to inhibit cell cycles, and to reduce the tumor growth in mice. *See* Examples 7-11. Generally, the use of disorazole compounds is described in the specification, paras. [0038]-[0042]. Specifically, Example 7 describes the use of disorazole compounds for their antiproliferative activities in a proliferation test on established tumor cell lines (Scuderio *et al.* Cancer Res. 1988, 48, 4827-4833): human cervical carcinoma cell line KB/HeLa, ovarian adenocarcinoma cell line SKOV-3 (ATCC HTB77), human glioblastoma cell line SF-268 (NCI 503138), lung carcinoma cell line NCI-H460 (NCI 503473) and human colon adenocarcinoma cell line RKOP 27. More importantly, Example 11 describes using a disorazole compound to treat NCI-H460 tumor xenograft-bearing nude mice, with a significant reduction in tumor growth even at doses which produced no weight decrease or mortality (*see* para. [0005]).

As the tested compounds are representative of the entire genus, one skilled in the art would recognize that Applicants have possession of the claimed methods of inhibition and treatment with disorazole compounds.

(B) ENABLEMENT

"Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.'" *In re Vaeck*,

947 F.2d 488, 495 (Fed. Cir. 1991). As discussed below, one skilled in the art, given the teachings in the specification, would be able to make and use disorazole compounds without undue experimentation.

With respect to the method of treatment claims, the Examiner stated that "the disclosure provides no indication of whether the compounds treat all cancers. To make clearer **the lack of enablement** for treatment of all cancer, extrinsic evidence is supplied by Draetta ... the data as presented are not sufficient to **enable** such claims" (emphases added). The Office Action, page 6.

Applicants would like to point out that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of Section 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970). Here, Applicants not only provide general guidance on the use of the compounds of the invention for the treatment of oncoses, benign or tumor diseases (*see* paragraphs [0038]-[0048]), but also present specific examples for *in vitro* testing the compounds of the invention for inhibition of the proliferation of various tumor cell lines (*see* Examples 7-8), for *in vitro* testing the compounds of the invention for inhibition of the polymerization of tubulin (*see* Example 9), for *in vitro* testing the compounds of the invention for inhibition of cell cycles (*see* Example 10), and for *in vivo* testing the compounds of the invention for inducing tumor growth in mice (*see* Example 11). "An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed or claimed method invention." *See* MPEP §2164.02. Thus, one person skilled in the art, provided with the general guidance and specific examples in the specification directed against a variety of tumors, would have a reasonable expectation that a

pharmaceutical composition containing the compounds of the invention would have efficacy in oncoses, benign or tumor diseases. Moreover, when the artisan is fully able to utilize claimed subject matter as described in the specification, clinical testing should not be made a prerequisite to patentability. *See In re Hartop*, 311 F.2d 249 (CCPA 1962) and *Ex parte Rubin*, 5 USPQ 2d 1461 (BPAI 1987).[3]

Furthermore, Applicants submit herewith (Exhibit A) a list of additional cell lines tested with disorazoles compounds A1 and E1 including tissues from pancreas, brain, ovarian, skin, lung, skeletal muscle, prostate, uterus, breast, and lymph.

For at least the foregoing reasons, Applicants submit claims 4-5, 9-13 and 18 are enabled.

Proviso Recited In Claims

"A proviso in the definition of X and Y has been noted. Applicant is requested to disclose the disclaimed prior art." *See* the Office Action, page 7. The proviso is to exclude the compound disorazole A1 (formula IV) (*see* the specification para [0036]), which has been described in the Hoefle reference (*id.* at para. [0004]). The Hoefle reference has been submitted to the Examiner in an IDS filed on February 6, 2004.

Related Applications

Applicants would like to bring the Examiner's attention to U.S. Patent Application Serial Nos. 11/486,140 (U.S. Publication No. 2007/0021480) and 11/850,747 (U.S. Publication No. 2008/0090758), each of which shares with the present application at least one common inventor.

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[3] The Examiner also stated that "there is no example to use the compound with another 'antitumor agent' or signal transduction inhibitors." The Office Action, page 6. However, "the absence of working examples will not by itself render the invention non-enabled." *See* MPEP §2164.02. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art would be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908 (CCPA 1970). Here, it is well known to one skilled in the art that it would be useful to combine an antitumor drug with another antitumor agent or signal transduction inhibitor, then the specification need not contain an example.

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CONCLUSION

In light of the foregoing, Applicants respectfully submit that all pending claims are now in condition for allowance.

It is believed that no other fees are necessitated by the present Reply. However, in the event that any additional fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-0923.

If the Examiner believes that a telephone conversation with Applicants' attorney would expedite allowance of this application, the Examiner is cordially invited to telephone the undersigned attorney at the number provided below.

Respectfully submitted,

Date: July 31, 2008

Q. Hong Xu (Reg. No. 52,378)
Goodwin Procter LLP
599 Lexington Avenue
New York, New York 10022
Tel. No.: (212) 813-8839
Fax No.: (212) 355-3333

Exhibit A

Cytotoxicity of various Disorazol derivatives

Cell line	Tissue	IC50 value in micromolar [µM] D-42803 Dis A1	D-42804 Dis D1	D-42805 Dis E1
ASPC1	Pancreas	0.0001	n.d.	0.00007
A172	Brain	0.0003	n.d.	0.0002
A2780	Ovarian	0.0009	n.d.	0.0006
A2780CIS	Ovarian	0.0006	n.d.	0.0003
A375	Skin	n.d.	n.d.	0.00008
A431	Skin	0.00006	n.d.	0.00005
A549	Lung	0.0001	n.d.	0.00006
L8	Skeletal muscle	n.d.	n.d.	0.0001
MDA-MB435	Prostate	0.0001	n.d.	0.00008
MESSA	Uterus	0.0004	n.d.	0.0005
MESSADX5	Uterus	0.0025	n.d.	0.0025
NCIH69	Lung	0.0022	n.d.	0.0005
PC3	Prostate	0.00007	n.d.	0.00003
SKMEL28	Skin	n.d.	n.d.	0.00006
T47D	Breast	0.0002	n.d.	0.0002
U118MG	Brain	0.0001	n.d.	0.00004
U373MG	Brain	0.00002	n.d.	0.00004
U937	Lymph	n.d.	n.d.	0.0001